Exhibit "N"

UNITED STATES OF AMERICA

DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

+ + +

CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

MEDICAL DEVICES ADVISORY COMMITTEE

+ + +

OBSTETRICS AND GYNECOLOGY MEDICAL DEVICES PANEL

+ + +

September 8, 2011
8:00 a.m.

Holiday Inn
2 Montgomery Village Avenue
Gaithersburg, Maryland

PANEL MEMBERS:

TOMMASO FALCONE, M.D.	Non-Voting Chair
ANDREW I. BRILL, M.D.	Non-Voting Member
ANN J. DAVIS, M.D.	Non-Voting Member
PAULA J. HILLARD, M.D.	Non-Voting Member
RICHARD CHAPPELL, Ph.D.	Temporary Non-Voting Member
CHARLES CODDINGTON, M.D.	Temporary Non-Voting Member
MICHAEL P. DIAMOND, M.D.	Temporary Non-Voting Member
ROSALIE DOMINIK, Dr.Ph.	Temporary Non-Voting Member
GEORGE FLESH, M.D.	Temporary Non-Voting Member
MARY PAT FITZGERALD, M.D.	Temporary Non-Voting Member
CHERYL IGLESIA, M.D., FACOG	Temporary Non-Voting Member
CHRISTINE SEARS, M.D.	Temporary Non-Voting Member
SUSAN KALOTA, M.D.	Temporary Non-Voting Member
DONALD R. MATTISON, M.D.	Temporary Non-Voting Member
REBECCA ROGERS, M.D.	Temporary Non-Voting Member
BARBARA BERNEY	Patient Representative
GARY L. DUERHRING, Ph.D.	Consumer Representative
SERGIO J. GADALETA, Ph.D.	Industry Representative
SHANIKA CRAIG, M.H.A., M.B.A.	Designated Federal Officer

experienced surgeons who understand the pelvic anatomy and surgical techniques necessary to successfully work with mesh in the vagina.

There has been great progress made in this area of women's health in a short amount of time. And while I'm not a regulatory expert, I do hope that we don't slow down the medical advances we have seen thus far by putting undue restrictions on these devices that have helped so many women.

We need to give women accurate information about the risks and benefits of every procedure so we ensure that they take advantage of the surgical option that may be in their best interests overall.

Thank you for your time.

DR. HINOUL: Thank you. Good morning. I'm Dr. Piet Hinoul, the Worldwide Medical Affairs Director for Women's Health and Urology of Ethicon. I came to Ethicon two years ago, and up until that time I was a practicing urogynecologic surgeon. I've performed of hundreds of transvaginal mesh procedures and traditional procedures to treat pelvic organ prolapse, and as a result, I have seen firsthand the clinical benefit this treatment option can provide women.

Today, I'm speaking on behalf of the Transvaginal Mesh Working Group through AdvaMed. In the next few minutes I would like to address the question that the FDA asked you to consider. I will highlight the data that demonstrate a favorable benefit/risk profile of transvaginal mesh

repair for prolapse, and I will also outline the clinical proposals that the working group is suggesting to continue to ensure the safety and effectiveness on both existing products and new products coming to the market.

Device manufacturers have been consistently improving these products and conducting studies on these devices since they first became available. The first five-year studies on transvaginal mesh kits are being reported upon and additional studies are underway. This is, of course, in addition to the rigorous bench and animal testing that occurred before surgeons ever used these meshes.

Today, to help you in your deliberations, we would like to provide context of how these devices are being used, our analysis of the data, as well as our proposals to further the progress that has already been made in this important field in female health.

As Dr. Sutherland has just explained, pelvic organ prolapse is a complex disease involving several anatomic compartments and different levels of disease, which can be addressed through different surgical options, each with their own potential merits and their own potential complications.

Patients and doctors need to consider all the factors we just mentioned, as well as the patient's medical history, the surgeon's training and experience, and available data on intervention, to make an informed decision on which surgical approach is best for that patient.

Transvaginal mesh, like all medical treatments, is not the optimal solution for everyone, but it will be for some.

Starting with the FDA's question on whether there is adequate assurance of effectiveness, current data demonstrate that transvaginal mesh is effective; first, because it demonstrates a statistically significant high anatomic cure rate than traditional surgeries; secondly, there is also significant improvement in quality of life measures that is comparable to traditional surgery.

The first measure of efficacy is anatomic cure, which is measured by the POP-Q score, and that is a measure that the National Institute of Health and multiple medical societies have determined is the most objective outcome measure. And we are aware of the ongoing scientific discussions regarding whether the current staging of pelvic organ prolapse actually correlates with the patient symptoms. Regardless of the outcome of the scientific discussions, anatomic assessment will remain a cornerstone in assessing prolapse.

Now, let's look at the literature addressing anatomic cure rates. Among the randomized controlled trials for pelvic organ prolapse, seven compared transvaginal polypropylene mesh to traditional vaginal surgery. These data clearly show that transvaginal mesh is efficacious in restoring pelvic floor anatomy. In fact, in five of the seven, the difference between the two were statistically significant. Even the two studies, by Dr. Iglesia and

Dr. Carey, that did not reach significance, trended in the same direction, showing higher efficacy for the mesh arm in their studies.

The second measure considered in the studies was quality of life, or often referred to as QoL. The quality of life improvements reported in these studies for mesh were both clinically and statistically significant. And in the studies, where improvement in both groups were compared, the improvements were similar.

Now, I would like to briefly focus on the largest randomized controlled trial conducted to date on transvaginal mesh. This landmark article, recently published in *The New England Journal of Medicine*, specifically addressed women with isolated anterior vault prolapse.

This was a multicenter study that followed 389 women, comparing mesh to traditional colporrhaphy. They used a compound outcome measure for defining success, looking at both anatomic cure as well as the most specific prolapse symptom, the feeling of bulge. This article reports on these endpoints at one-year follow-up.

Women using mesh had an 82 percent anatomic cure rate as opposed to 48 percent cure rate in the traditional native repair arm. Mesh kits were superior for symptomatic outcome as well: 75 percent in favor of mesh versus 62 percent for colporrhaphy. The compound measure thus yielded a significant difference in favor of mesh, with a combined anatomic and functional success of 61 versus 35 percent.

Therefore, this study provides Level I evidence and is a clear indication that transvaginal mesh kits are a valuable treatment option, from both an anatomic as well as a functional viewpoint, for women suffering from anterior vaginal wall prolapse.

So we looked at effectiveness. Now, let's turn our attention to safety.

The FDA poses the question of whether there's adequate assurance of safety of transvaginal mesh for prolapse. The data demonstrates that there is adequate assurance of safety when we consider the two incidents of serious adverse events. Serious adverse events that are mesh-specific are very low.

Looking at the FDA's MAUDE database, which is designed to identify new events and signals, there have been new adverse events related to vaginal mesh identified since the initial introduction of these products. Although rates vary, the types of events remain the same.

We know from the literature that exposures are the most commonly reported adverse events for transvaginal mesh kits. We believe it's important to understand an essential distinction between mesh exposure, where a piece of mesh is exposed into the vagina, and mesh erosion, where we are actually referring to a perforation into a hollow organ by the mesh. Not differentiating between the two may lead one to over-interpret its clinical importance.

Mesh erosion complications are so rare that we learn about them in the literature through case reports. The long-term data we have for sacrocolpopexy, which uses exactly the same material as these mesh kits, has long established this.

For transvaginal meshes, when exposures occur, nearly half can be treated nonsurgically, as shown in a large meta-analysis by the Society of Gynecologic Surgeons, of 10,000 women treated by mesh.

One of the most important questions we need to ask ourselves is also why these adverse events are occurring. And the risk factors for mesh exposures are becoming more and more apparent. Several studies published this year show that hysterectomy, patient age, smoking, diabetes, and surgeon experience predispose patients to mesh exposure. Patient selection and risk factors, appropriately stated in the device's labeling, as well as the surgeon's training, are therefore part of our proposal.

Another adverse event that has attracted the attention is the occurrence of dyspareunia, or painful intercourse. It's important to note that dyspareunia is inherent to the condition of prolapse. And as you can see in the study quoted by Lowman, dyspareunia at baseline and new onset of dyspareunia post-intervention is prevalent for all treatment options.

While there has been a lot of focus on the complications of transvaginal mesh, it is important to note that the total complication rate for traditional repair, sacrocolpopexy, and mesh kits are all very similar, at 15, 17

and 15 percent, respectively, as shown in this meta-analysis on procedures addressing apical support.

Note that the total reoperation rate is indeed higher for the mesh kits, but most of these constitute ambulatory procedures for mesh exposure, while those for traditional repair and sacrocolpopexy are often major in patient operative procedures to treat wound problems, fistula injury, and bleeding.

Let us know turn to the question of whether the benefits of transvaginal mesh outweigh the risks. The data says yes. The benefits are clear in the areas of anatomic restoration and quality of life measures.

Risk is well defined. There have been no new events identified since the introduction of the products, and their rates remain low.

This is a complicated disease with a variety of presentations and available interventions. As I noted earlier, these treatment options are not one size fits all, nor are they each the most appropriate for all patients. It comes down to the surgeon individualizing the patient's care to her specific condition, but also to the patient-specific goals and expectations.

So turning to the FDA's questions regarding whether clinical studies should be performed premarket for transvaginal mesh, our position is yes, because, for transvaginal products, clinical data should continue to be generated for all new products, to assure new products remain as safe and effective as the current interventions.

We also want to make sure, however, that we are clear on what a clinical trial is meant to achieve. The appropriate trial design must be developed in conjunction with surgeons, manufacturers, and FDA because we firmly believe that one trial design will not apply to all new pelvic floor devices. The type of study will depend on the specific question of safety and efficacy asked, depending on the product differences from current products.

The study will also have to address the indication for use and the target population. Equally important can be to confirm whether key claims are met or when specific research questions need to be answered.

For these reasons, we have reservations about the FDA study design proposal because we don't believe that one clinical design can fit all. We agree that multiple efficacy endpoints assessing both functional and anatomical outcomes are needed. However, because of the low rate of adverse events, a trial powered for non-inferiority would require an unacceptably large number of patients in order to meet that endpoint, with little gain in patient protection.

There are also some practical limitations regarding a surgical randomized controlled trial design that we must consider. First, surgeon and patient preference to one type of surgery over another will influence recruitment. Also, ensuring that the control arm, the traditional repair, is performed in a standard fashion is not always easy. And lastly, blinding the assessor has proven to be difficult, as incision size and adverse events reveal

what type of surgery was actually performed.

Therefore, we believe that for the introduction of the majority of new devices, a single-arm, prospective trial with multiple efficacy endpoints assessing functional anatomy will appropriately address the questions regarding continued safety and efficacy.

As I mentioned, we feel the study should be powered to address these multiple efficacy endpoints that assess both anatomy and symptoms.

In conclusion, we believe the benefit/risk profile of transvaginal mesh is comparable to traditional surgeries. In fact, the data demonstrate that transvaginal mesh is superior or equivalent to traditional surgery with respect to anatomy and is comparable in quality of life measures.

Serious adverse events, including mesh erosion, not to be confused with exposures, are rare. And mesh exposure, the most common adverse event, is usually minor and well manageable.

Nevertheless, device manufacturers are committed to collecting long-term data to further elucidate the benefit/risk ratio and to perform premarket clinical trials for new devices for this indication.

As a gynecologic surgeon who has seen firsthand the positive difference these procedures can make in a woman's life, and now as a medical director committed to ensuring safety and efficacy of these products, I want to make sure that this is an option that remains available for the

patients that need it.

I would now like to introduce Ginger Glaser, the Senior Director of Global Quality and Regulatory Affairs at American Medical Systems, to discuss our regulatory proposals in greater detail. Thank you.

MS. GLASER: Thank you, Dr. Hinoul. And good afternoon, everyone. I would like to focus my presentation on the question FDA is posing to you regarding the appropriate regulatory pathway for transvaginal mesh.

As the members of the Advisory Committee have seen from the briefing booklets, due to their evaluation of the literature and MAUDE data, FDA believes additional regulatory controls are needed for this product category.

As Dr. Hinoul described, these devices have been shown to be a safe and effective treatment option for women with prolapse.

We do agree that the early experience with these devices, as is common with all new devices, has identified areas for further study that may facilitate the continued achievement of possible optimal patient outcomes. Thus, we agree that FDA should utilize additional regulatory tools that are available within the Class II 510(k) process to ensure such information is collected and that patients and physicians receive the information that they need to continue to use the product safely and effectively.

In fact, of the types of controls that FDA has referenced, we